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- b) at least one eukaryotic based nucleic acid sequence that encodes a wild-type gene product controlled by a eukaryotic based cis-acting regulatory sequence heterologous to the wild-type gene product[; and
- c) at least one eukaryotic based nucleic acid sequence that encodes a wild-type gene product],

said virus vector having the property of regulating cell specific expression of said nucleic acid sequence or nucleic acid sequences upon stable transduction of a target mammalian cell.

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9. (amended) A recombinant adeno-associated virus vector of Claim [8] 1 wherein said nucleic acid sequence or nucleic acid sequences encodes at least one human gene protein, chosen from the human globin gene cluster.

10. (amended) A recombinant adeno-associated virus vector of Claim [5] 48 wherein said eukaryotic *cis*-acting regulatory sequence is chosen from the region located from about hypersensitive site I to about hypersensitive site VI, in association with the human globin gene cluster.

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12. (amended) A recombinant adeno-associated virus vector of Claim [11] 48 wherein said nucleic acid sequence or nucleic acid sequences encodes at least one human gene protein, chosen from the human globin gene cluster.

sub 63

16. (amended) A recombinant adeno-associated virus vector of Claim [15] 4 wherein said *cis*-acting regulatory sequence comprises hypersensitive site II, associated with the human globin gene cluster.

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17. (amended) A recombinant adeno-associated virus vector of Claim [16] 4 wherein said nucleic acid sequence encodes a human globin protein ^Agamma globin.

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19. (amended) A recombinant adeno-associated virus vector of Claim [18] 4 wherein said immune cell is chosen from the group consisting of a human hematopoietic stem cell, a human myeloid progenitor cell and a human erythroid progenitor cell.



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21. (amended) A recombinant adeno-associated virus vector of Claim [22] 48 wherein said mammalian cell is an [target] immune cell [is] chosen from the group consisting of a human hematopoietic stem cell, a human myeloid progenitor cell and a human erythroid progenitor cell.

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27. (twice amended) A recombinant adeno-associated virus vector, which comprises:

- a) at least a portion of the adeno-associated virus genome; and
- b) a eukaryotic based nucleic acid sequence that encodes a wild-type gene product controlled by a eukaryotic based cis-acting regulatory sequence heterologous to the wild-type gene product [; and]
- c) a eukaryotic based nucleic acid sequence that encodes a wildtype gene product],

said virus vector having the property of regulatory cell specific expression of said nucleic acid sequence or nucleic acid sequences upon stable transduction of a human primary hematopoietic cell.

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31. (amended) A recombinant adeno-associated virus vector of Claim [30] 27 wherein said nucleic acid sequence encodes a human globin protein, chosen from the human globin gene cluster.

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46. (amended) The recombinant adeno-associated virus vector of Claim 1 in which the portion of the adeno-associated virus genome comprises at least those nucleotide sequences encoding the inverted terminal repeats.

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47. (amended) The adeno-associated virus vector of Claim 27 [is] in which the portion of the adeno-associated virus genome comprises at least those nucleotide sequences encoding the inverted terminal repeats.

Please add Claim 48, as follows:

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--48. (new) A recombinant adeno-associated virus vector comprising:

- a) at least a portion of the adeno-associated virus genome;

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b) a eukaryotic based nucleic acid sequence that encodes a wild-type gene product controlled by a eukaryotic based *cis*-acting regulatory sequence and
c) lacking a selectable marker,

said virus vector having the property of regulating cell specific expression of said nucleic acid sequence or nucleic acid sequences upon stable transduction of a mammalian cell.--

REMARKS

Claims 1-35, 39, 46 and 47 were pending in the instant application. Applicants acknowledge that Claims 40 and 41 added in the amendment filed December 9, 1998 were misnumbered and have been renumbered Claims 46 and 47. Applicants have canceled Claims 2, 3, 5, 6, 13-15, 18, 22-24, 32, 34 and 35, without prejudice to the Applicants right to pursue the subject matter of the canceled claims in related applications. Claims 1, 9, 10, 12, 16, 17, 19, 21, 27, 31, 46, and 47 have been amended and new Claim 48 has been added to more particularly point out and distinctly claim the subject matter of the present invention. The amendments and new claims are fully supported by the instant specification, *e.g.*, see page 21, line 22 to page 22, line 27, and do not represent new subject matter. With entry of this amendment, therefore, Claims 1, 4, 7-12, 16-17, 19-21, 25-31, 33, 39, and 46-48 will be pending. For the Examiner's convenience, a copy of the pending claims as amended is annexed hereto as Exhibit A.

The new independent claim, and claims dependent therefrom, are directed to recombinant AAV vectors comprising a eukaryotic nucleic acid sequence encoding a wild-type gene product controlled by a eukaryotic based *cis*-acting regulatory element. In particular, independent Claim 1 covers recombinant AAV vectors comprising a eukaryotic based *cis*-acting regulatory element heterologous to the wild-type gene product which regulates cell-specific expression of the wild-type gene upon stable transduction of a target mammalian cell. Independent Claim 27 covers recombinant AAV vectors comprising a eukaryotic based *cis*-acting regulatory element heterologous to the wild-type gene product which regulates cell-specific expression of the wild-type gene upon stable transduction of a human primary hematopoietic cell. Independent Claim 48 covers recombinant AAV vectors comprising a eukaryotic based *cis*-acting regulatory element and lacking a selectable marker.